

Appl. No. 10/091,300
Amtdt. dated Jun. 22, 2004
Reply to Office Action dated Dec. 25, 2003

Docket No. 11245/46211

I. AMENDMENTS TO THE SPECIFICATION

Please replace paragraph [01] with the following amended paragraph.

[01] This application is a continuation-in-part of Application No. 09/798,689, filed March 2, 2001, ~~pending~~issued, which is a continuation-in-part of Application No. 09/401,163, filed on September 22, 1999, now U.S. Patent No. 6,365,157~~pending~~, which is a continuation of Application No. 08/967,113 filed on November 10, 1997, now U.S. Patent No. 6,448,077~~pending~~, which is a continuation-in-part of Patent Number 5,861,499 filed September 3, 1996, which is a continuation-in-part of Application No. 08/476,533 filed June 7, 1995, abandoned, which is a continuation of Patent Number 5,840,301 filed October 20, 1994, which is a continuation-in-part of Application No. 08/196,041 filed February 10, 1994, abandoned. The entire disclosures of the aforementioned prior applications are incorporated herein by reference.

Please replace paragraph [91] with the following amended paragraph.

[91] Many other VEGFR antagonists are known in the art. Some examples of VEGFR antagonists are described in U.S. Patent Nos. 5,185,438; 5,621,090; 5,283,354; 5,270,458; 5,367,057; 5,548,065; 5,747,651; 5,912,133; U.S. Application Nos. 07/813,593; 07/906,397; 07/946,507; 07/977,451; 08/055,269; 08/252,517; 08/601,891; 09/021,324; 09/208,786, abandoned; and 09/919,408, pending (all to Lemischka et al.); U.S. Patent No. 5,840,301 (Rockwell et al.); U.S. Patent Nos. 5,861,499; 5,874,542; 6,448,077; 5,955,311; 6,365,157; and U.S. Application Nos. 08/706,804; 08/866,969; 08/967,113; 09/047,807; 09/401,163; and 09/798,689, allowed (all to Rockwell et al.); U.S. Application No. 09/540,770, pending (Witte et al.); and PCT/US01/06966 (Liao et al.). U.S. Patent No. 5,861,301 (Terman et al.), Terman et al. Oncogene 6: 1677-1683 (September 1991), WO 94/10202 (Ferrara et al.), and WO 95/21865 (Ludwig) disclose VEGFR antagonists and, specifically, anti-VEGFR-2 antibodies. In addition, PCT/US95/01678 (Kyowa Hakko), describes anti-VEGFR-2

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antibodies. Anti-VEGFR antibodies are also described in U.S. Application No. 09/976,787, pending (Zhu et al.). U.S. Patent Nos. 6,177,401 (Ullrich et al.), 5,712,395 (App et al.), and 5,981,569 (App et al.) describe VEGFR antagonists that are organic molecules. In addition, bi-specific antibodies (BsAbs), which are antibodies that have two different antigen-binding specificities or sites, directed to KDR (VEGFR-2) and VEGFR-1 are known. See, e.g., U.S. Application No. 09/865,198, abandoned (Zhu); 60/301,299 (Zhu), now U.S. Application No. 10/482,630, pending.

Please replace paragraph [168] with the following amended paragraph.

[168] In one alternative embodiment, the EGFR antagonist and the VEGFR antagonist can be administered in combination with one or more antineoplastic agents. See, e.g., U.S. Patent No. 6,217,866 (Schlessinger et al.) (Anti-EGFR antibodies in combination with antineoplastic agents); U.S. Application No. 09/312,286, abandoned (Waksal et al.) (Anti-EGFR antibodies in combination with radiation). Any suitable antineoplastic agent can be used, such as a chemotherapeutic agent or radiation. Examples of chemotherapeutic agents include, but are not limited to, cisplatin, doxorubicin, paclitaxel, irinotecan (CPT-11), topotecan or a combination thereof. When the antineoplastic agent is radiation, the source of the radiation can be either external (external beam radiation therapy – EBRT) or internal (brachytherapy – BT) to the patient being treated. The dose of antineoplastic agent administered depends on numerous factors, including, for example, the type of agent, the type and severity tumor being treated and the route of administration of the agent. It should be emphasized, however, that the present invention is not limited to any particular dose.